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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/509,362	04/15/2005	Elfi Biedermann	25846-0005	3950

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EXAMINER	
PACKARD, BENJAMIN J	

ART UNIT	PAPER NUMBER
1612	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/509,362	BIEDERMANN ET AL.	
	Examiner	Art Unit	
	Benjamin Packard	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 April 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15-30* is/are pending in the application.

4a) Of the above claim(s) *27 and 28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-26,29,and 30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1pg (1/12/2005)*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Election/Restrictions

Applicant's election with traverse of Group I, claims 15-26 and 29-30, as well as the elections of the compound N-[4-(1-benzoyl-piperidin-4-yl)-butyl]-3-(pypridin-3-yl)-acrylamide and inflammatory disorder in the reply filed on 4/25/2008 is acknowledged. The traversal is on the ground(s) that while the compound is known, the special technical feature should be the administration of the compound. This is not found persuasive because Biedermann (WO 97/486696) was cited to show that the instant class of pharmaceutical compounds was known, therefore administration of the same would have been obvious. As such, there is no special technical feature common between the two groups of the class of compounds.

The requirement is still deemed proper and is therefore made FINAL.

Claims 27-28 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Note, because the instantly elected compound appears to be free of the prior art for treatment of the specifically claimed diseases of instant claims 29-30, the search was extended to an additional claimed compound for these claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 15-26, 29 and 30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for reducing undesired angiogenesis and thus treating a disease or medical condition selected from rheumatoid arthritis, inflammatory disorder, macular degeneration, psoriasis, retinopathy, preneoplastic lesions, and hyperplasia, does not reasonably provide enablement for the prevention or inhibition of angiogenesis generally. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

To be enabling, the specification of the patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557, 1561 (Fed. Cir. 1993). Explaining what is meant by "undue experimentation," the Federal Circuit has stated:

> The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention. PPG v. Guardian, 75 F.3d 1558, 1564 (Fed. Cir. 1996).

The factors that may be considered in determining whether a disclosure would require undue experimentation are set forth by In re Wands, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing Ex parte Forman, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary,

2) the amount of direction or guidance provided,

3) the presence or absence of working examples,

4) the nature of the invention,

5) the state of the prior art,

6) the relative skill of those in the art,

7) the predictability of the art, and

8) the breadth of the claims.

These factors are always applied against the background understanding that scope of enablement varies inversely with the degree of unpredictability involved. In re Fisher, 57 CCPA 1099, 1108, 427 F.2d 833, 839, 166 USPQ 18, 24 (1970). Keeping that in mind, all Wands factors have been considered and the following factors that are relevant to the instant fact situation for the following reasons:

1. The nature of the invention, state and predictability of the art, and relative skill level

The invention relates to treatment and prevention of disease, particularly treating inflammatory disorders. The relative skill of those in the art is high, that of an MD or PHD. That factor is outweighed, however, by the difficult nature of the art. As illustrative of the state of the art, the examiner cites Carmeliet et al (Nature, Vol. 407, 14 Sept 2000, 249-257). On page 255, the Authors point out that even if one molecule is blocked, such as VEGF, the cells may switch to another molecule. Thus there is no single pathway to inhibit angiogenesis generally.

2. The breadth of the claims

The claim relates to inhibiting "angiogenesis" as a general biochemical.physiological phenomenon, besides the treatment of certain angiogenesis-related disease states, such as inflammatory disorder.

3. The amount of direction or guidance provided and the presence or absence of working examples

The specification provides no direction or guidance for the prevention of the disease or disorders. No reasonably specific guidance is provided concerning useful therapeutic protocols for disorders, other than reducing undesired angiogenesis associated with murine renal cell carcinoma. The latter is corroborated by the working examples.

4. The quantity of experimentation necessary

Because of the known unpredictability of the art, and in the absence of experimental evidence, no one skilled in the art would accept the assertion that the instantly claimed agents could be predictably used for the prevention of the possible diseases and disorders as inferred by the claim and contemplated by the specification. Accordingly, the instant claims do not comply with the enablement requirement of §112, since to practice the invention claimed in the patent a person of ordinary skill in the art would have to engage in undue experimentation, with no assurance of success.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 15-25 are rejected under 35 U.S.C. 102(b) as being anticipated by Biedermann et al (WO 97/48397).

The instantly elected compound is shown as a preferred embodiment at page 82, compound number 259. The function of the compounds is disclosed for the treatment of tumors (page 1 first paragraph).

The inhibition of angiogenesis generally would have been reasonably expected to be inherent, given that angiogenesis is the building of new blood vessels which occurs regularly in the human body, such as healing of wounds.

Claims 15-25 are rejected under 35 U.S.C. 102(b) as being anticipiated by Nishikawa et al (J. Med. Chem, 1989, 32:583-593, see Applicants' IDS dated 1/12/2005).

Nishikawa et al describes the administration of the instantly claimed compounds in rat models (page 585). In particular, [4-(1-benzylpiperazin-4-yl)-butyl]-3-(pyridin-3-yl)-propionamide is disclosed on page 585 at chart II, compound 18a.

The inhibition of angiogenesis generally would have been reasonably expected to be inherent, given that angiogenesis is the building of new blood vessels which occurs regularly in the human body, such as healing of wounds.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary.

Claims 15-26 and 29-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nishikawa et al (J. Med. Chem, 1989, 32:583-593, see Applicants' IDS dated 1/12/2005) in view of Daotai et al (Homeostasis, Thrombosis, and Vascular

Biology, Blood, 1 April, 2000, 95:7, see Applicants' IDS dated 1/12/2005) and Colavitti et al (Journal of Biological Chemistry, Vol 277, No 2, Feb 1, 2002, 3101-3108, see Applicants' IDS dated 1/12/2005).

Nishikawa et al describes the activity of the instantly claimed compounds as lipoxygenase inhibitors. In particular, [4-(1-benzylpiperazin-4-yl)-butyl]-3-(pyridin-3-yl)-propionamide is disclosed on page 585 at chart II, compound 18a.

Daotai et al discloses the role of lipoxygenase inhibitors for treating angiogenesis mediated diseases, such as inflammation and reitnopathy. Moreover it is pointed out that a lipoxygenase inhibitor can counteract the effects of VEGF (see page 2310, column 2, paragraph 4; column 1, paragraph 1).

Therefore, knowing that the compounds of instant formula 1 are lipoxygenase inhibitors and being aware that lipoxygenase inhibitors are useful for inhibiting angiogenesis and for reducing the effects of VEGF[1], one of ordinary skill in the art would have found it obvious to use the pyridine derivatives of formula 1, and in particular the compounds disclosed in the secondary reference, for reducing angiogenesis.

This teaching would strengthen the motivation of the person skilled in the art, to use the same compounds, counteracting the effects of VEGF and known for treating inflammations and tumors, also for reducing angiogenesis.

Conclusion

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Benjamin Packard whose telephone number is 571-270-3440. The examiner can normally be reached on M-F 8-3:45 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick Krass can be reached on 571-272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Benjamin Packard/
Patent Examiner, Art Unit 1612

/Frederick Krass/
Supervisory Patent Examiner, Art Unit 1612

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[1] Colavitti et al points out VEGF is the major angiogenic factor produced by cells (see Colavitti et al: page 3101, column. 2, paragraph 3).